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The mechanism of β-amyloid peptide influence on the retrograde axon transport

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Abstract

Impairment of axon transport is widespread and early event in a number of neurodegenerative diseases. The goal of study is to investigate the mechanisms of retrograde axon transport impairment in mouse spinal motoneurons after application of β-amyloid peptide (βAP) (25-35) on the central stump of transected sciatic nerve. Retrograde fluorescent tracer Fluorogold (5%), β AP (25-35) (10-6 M), or mix was applied to the proximal stump of the transected sciatic nerve of mouse under the general anesthesia. At 24 hours after surgery lumbar spinal cord was processed for morphometric and immunohistochemical analysis. The amount of Fluorogold-positive motoneurons at control was 1223,7±162,7 (n = 7), whereas after application of βAP(25-35) - 393,2±85,3 (n = 5, p < 0,01), which certifies pronounced inhibition of retrograde axonal transport. Staining with polyclonal antibodies against caspase-3 did not reveal motoneurons in apoptotic state. Staining with monoclonal antibodies against the β AP (25-35) was negative both at operated and intact sides of spinal cord. Thus, revealed inhibitory action of β AP (25-35) on the retrograde axon transport is not related to apoptotic death of neurons or accumulation of β AP (25-35) inside the neuronal soma, but, evidently, is mediated by intraaxonal effects. Obtained data has great importance for understanding of mechanisms of Alzheimer's disease pathogenesis.

Keywords

β-Amyloid peptide, Alzheimer's disease, Caspase-3, Motoneuron, Retrograde axon transport